

Application No. 09/211,715
Reply to Office Action of November 20, 2002

May 7, 2003
S&L File No. P26,835 USA

REMARKS

Claims 2, 3, 7-11, 20-23 and 25 are pending in the application. Claims 2 and 3 have been cancelled herein without prejudice. Applicants reserve the right to pursue the subject matter of claims 2 and 3 in a continuing application that claims the same benefit of priority as the subject application.

Claims 8, 9, 10, 11, 20 and 25 have been amended. Support for the amendment to the specification and claims 8, 10, 11, and 20 can be found, for example, at page 11, lines 13-14. Support for the amendment to claim 9 can be found, for example, at page 12, line 29. Support for the amendment to claim 25 can be found, for example, in the claims as filed and in the specification at page 8, lines 20-23. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested. A marked up version of the amended claims is provided in Appendix A attached hereto.

Applicants have carefully reviewed the Office Action and respectfully traverse all grounds of objection and rejection to the application for the reasons that follow.

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Rejection Under 35 U.S.C. § 112, First Paragraph

The objection to the specification and rejection of claims 2 and 3 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed.

The Office Action acknowledges that the specification is enabling for Y-I-R containing peptides or closely related analogues. However, the Office Action states that the specification does not provide enablement for a general formula recited in claims 2 and 3.

Applicants maintain that the specification provides sufficient guidance to enable claims 2 and 3. In addition, since claims 2 and 3 have been cancelled herein, the rejection of claims 2 and 3 under 35 U.S.C. § 112, first paragraph, has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claims 2 and 3 under 35 U.S.C. § 112, first paragraph, be removed.

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Rejection Under 35 U.S.C. § 112, Second Paragraph

The objection to the specification and rejection of claims 2, 3, 9 and 11 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting the term "Leu-OH" is respectfully traversed.

Applicants believe that claim 11 has been rejected in error because claim 11 does not recite the term "Leu-OH". Claims 2 and 3 have been cancelled herein. Therefore, only the rejection of claim 9 remains.

The Office Action states that the term "Leu-OH" is not clear regarding whether or not the hydroxyl group is linked to the alpha carbon of leucine. Applicants maintain that the term "Leu-OH" is clear and definite to one skilled in the art as a notation used to emphasize that the C-terminus of leucine is not modified. Nevertheless, in order to further prosecution, Applicants have amended claim 9 replacing the term "Leu-OH" with "Leu." Accordingly, Applicants respectfully request that the rejection of claims 2, 3, 9 and 11 under 35 U.S.C. § 112, second paragraph, be removed.

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Rejection Under 35 U.S.C. § 102(e) and 103(a)

The objection to the specification and rejection of claims 2 and 3 under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, as obvious under 35 U.S.C. § 103(a) over Brunck, T.K. et al. (U.S. Patent No. 5,739,112) is respectfully traversed.

Applicants maintain that U.S. Patent No. 5,739,112 does not teach or suggest the claimed invention. In addition, since claims 2 and 3 have been cancelled herein, the rejection of claims 2 and 3 under 35 U.S.C. § 102(e) or 35 U.S.C. § 103(a) has been rendered moot. Accordingly, Applicants respectfully request that the rejection of claims 2 and 3 under 35 U.S.C. § 102(e) or 35 U.S.C. § 103(a), be removed.

Rejection Under Obviousness Type Double Patenting

The rejection of claims 2, 3, 8-10, 21-23, and 25 under the doctrine of obviousness-type double patenting, as allegedly unpatentable over claims in U.S. Patent No. 5,849,510, respectfully is traversed.

Applicants maintain that the rejected claims are distinct and non-obvious over U.S. Patent No. 5,849,510. Nevertheless, in order to further prosecution of the

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subject application, Applicants submit herewith a terminal disclaimer disclaiming the terminal part of any patent granted on the subject application that would extend beyond the expiration date of U.S. Patent No. 5,849,510. In view of the terminal disclaimer submitted herewith, Applicants respectfully request that the Examiner remove the obviousness-type double patenting rejection of claims 2, 3, 8-10, 21-23, and 25 over claims in U.S. Patent No. 5,849,510.

Objection to Claim

The Office Action states that the disclosure is objected to because of the following informalities: claim 10 recitation "-Pal(3)Me" appears to be a misspelling. Claim 10, as well as claims 8, 11, 20, and Table 6 in the specification which recite the term "-Pal(3)Me" have been amended per the Examiner's suggestion to "-PalMe(3)."

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CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent with any questions in regard to this application.

Respectfully submitted,

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APPENDIX A

In the specification:

Please replace Table 6 which begins at page 96, line 10 and ends on page 101, line 2 with the following.

TABLE 6

1. $\text{CF}_3\text{C}(\text{O})-(\text{iBu})\text{Phe}(\text{NH}_2)\text{-Chg-Arg-Leu-Pro-NH}_2$
2. $\text{Ac-pAph-Chg-Arg-Pen}(\text{CH}_2\text{COOH})\text{-Pro-NH}_2$
3. $\text{Ac-pAph-Ile-Arg-Leu-Pro-NH}_2$
4. $\text{Ac-pAph-Chg-Dab}(\text{CH}=\text{N}(\text{CH}_3)_2)\text{-Leu-Pro-NH}_2$
5. $\text{CF}_3\text{C}(\text{O})-(\text{iBu})\text{Nal}(2)\text{-Chg-Arg-Leu-Pro-NH}_2$
6. $\text{Ac-Phe}(3\text{I},4\text{NH}_2)\text{-Chg-Arg-Leu-Pro-NH}_2$
7. $\text{CF}_3\text{C}(\text{O})\text{-Tyr-Chg-Arg-Leu-Pro-NH}_2$
8. $(5\text{-benzimidazolyl})\text{-Phe}(\text{NH}_2)\text{-Chg-Arg-Leu-Pro-NH}_2$
9. $\text{CF}_3\text{C}(\text{O})-(\text{iBu})\text{Tyr-Ile-Arg-Leu-Pro-NH}_2$
10. $\text{Ac}-(\text{Chx-CH}_2)\text{Tyr-Ile-Arg-Leu-Pro-NH}_2$
11. $\text{D-Tyr-Chg-Arg-Leu-Pro-NH}_2$
12. $\text{Ac-Trp-Chg-Arg-Leu-Pro-NH}_2$
13. $(2\text{-benzofuroyl})\text{-Tyr-Chg-Arg-Pen-Pro-NH}_2$
14. $(2\text{-benzofuroyl})\text{-pAph-Chg-[Pal(3)Me]PalMe(3)-Pen}(\text{CH}_2\text{COOH})\text{-Pro-NH}_2$
15. $\text{Ac-pAph-Chg-Arg-Cys}(\text{CH}_2\text{COOH})\text{-Pro-NH}_2$
16. $(\text{Alloc})\text{-pAph-Chg-Arg-Leu-Pro-NH}_2$
17. $(2\text{-benzofuroyl})\text{-pAph-Chg-Arg-Pen}(\text{CH}_2\text{COOH})\text{-Pro-NH}_2$
18. $\text{Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-Pen}(\text{CH}_2\text{COOH})\text{-Pro-NH}_2$

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19. Ac-pAph-Chg-Arg-Leu-Pro-NH₂
20. pAph-Chg-Arg-Leu-Pro-NH₂
21. Ac-pAph-Chg-Arg-(HOOC-CH₂)Gly-Pro-NH₂
22. Ac-pAph-Chg-Arg(HOOC-CH₂-CH₂)Gly-Pro-NH₂
23. Ac-pAph-Chg-Arg-Gla-Pro-NH₂
24. Ac-pAph-Chg-Arg-Cys(CH₂-COOH)-Pro-NH₂
25. Ac-Pal(4)Me-Chg-Arg-Leu-Pro-NH₂
26. Ac-(iBu)Nal(2)-Chg-Arg-Leu-Pro-NH₂
27. Ac-Phe(p-CONH₂)-Chg-Arg-Leu-Pro-NH₂
28. Ac-pAph-Chg-Arg-N[1(1,3-dicarboxy)propyl]Gly-Pro-NH₂
29. Ac-pAph-Chg-Dap(CH=N(CH₃)₂)-Leu-Pro-NH₂
30. (2-quinolinoyl)-Phe(NH₂)-Chg-Arg-Leu-Pro-NH₂
31. Ac-pAph-Chg-Arg-N(carboxymethyl)Gly-Pro-NH₂
32. Ac-pAph-Chg-Arg-(carboxyethyl)Gly-Pro-NH₂
33. Ac-mAph-Chg-Arg-Leu-Pro-NH₂
34. Alloc-pAph-Chg-[Pal(3)Me]PalMe(3)-Pen(CH₂COOH)-Pro-NH₂
35. Ac-pAph-Chg-Arg-N[1(1,3-dicarboxy)propyl]Gly-Pro-NH₂
36. Ac-pAph-Ile-Arg-Leu-Pro-NH₂
37. Ac-Phe(pNH₂)-Chg-Arg-(Me)Leu-Pro-NH₂
38. Ac-(Chx-CH₂)Tyr-Chg-Arg-Leu-Pro-NH₂
39. (3-pyridoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
40. (3-pyridoyl)-Nal(2)-Chg-Arg-Leu-Pro-NH₂
41. Ac-Pal(4)Me-Chg-Pal(4)Me-Leu-Pro-NH₂
42. Alloc-pAph-Chg-Arg-Leu-Pro-NH₂
43. (4-isoquinolinoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
44. Ac-pAph-Cha-[Pal(3)Me]PalMe(3)-(Me)Leu-Pro-NH₂

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45. Ac-pAph-Chg-[**Pal(3)Me**]**PalMe(3)**-Leu-Pro-NH₂
46. (2-naphthyl-CH₂)Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
47. (5-pyrazinoyl)Nal(2)-Chg-Arg-Leu-Pro-NH₂
48. (Benzoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
49. Ac-(2-methylpentanyl)-Tyr-Ile-Arg-Leu-Pro-NH₂
50. (2-pyridonyl)Phe(pNH₂)Chg-Arg-Leu-Pro-NH₂
51. (Benzoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
52. Ac-pAph-Chg-[**Pal(3)Me**]**PalMe(3)**-Leu-Pro-NH₂
53. Ac-(2-methylpentyl)Tyr-Ile-Arg-Leu-Pro-NH₂
54. Ac-(iBu)Phe(pCN)-Chg-Arg-Leu-Pro-NH₂
55. Ac-(2-methylbutyl)Tyr-Ile-Arg-Leu-Pro-NH₂
56. Ac-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
57. Ac-Phe(pNH₂)-Chg-Arg-Leu-Hyp-NH₂
58. Ac-Tyr-Chg-Arg-Leu-Pro-NH₂
59. (2-naphthylsulfonyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
60. (2-methylbenzyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
61. (2-benzofuroyl)-Phe(pNH₂)-Chg-Dab(CH=N(CH₃)₂)-Leu-Pro-NH₂
62. Ac-(cyclopentenyl-CH₂)Tyr-Ile-Arg-Leu-Pro-NH₂
63. Ac-Pal(4)Me-Chg-[**Pal(3)Me**]**PalMe(3)**-Leu-Pro-NH₂
64. Ac-(iBu)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂
65. Ac-(Chx-CH₂)-Tyr-Ile-Arg-Leu-Pro-NH₂
66. Ac-pAph-Chg-Arg-Leu-NH₂
67. Ac-pAph-Chg-Arg-Leu-OH
68. (2-benzofuroyl)-pAph-Chg-[**Pal(3)Me**]**PalMe(3)**-NH₂
69. Ac-(iBu)Phe(pNH₂)-Chg-Arg-NH₂
70. Alloc-pAph-Chg-[**Pal(3)Me**]**PalMe(3)**-NH₂

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71. (2-quinolinoyl)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂
72. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH(1-methoxycarbonyl)-1-cyclohexyl
73. Ac-pAph-Chg-Arg
74. (2-pyridoyl)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂
75. CF₃C(O)-(iBu)Phe(pNH₂)-Chg-Arg-NH₂
76. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(1-methoxycarbonyl)-1-cyclopentyl
77. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(4-methoxycarbonyl
-cyclohexyl)methyl
78. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(3-thienyl-2
-carboxylic acid methyl ester)
79. Ac-pAph-Chg-Arg-NH₂
80. CF₃C(O)-(iBu)Tyr-Chg-Arg-OH
81. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(4-methoxycarbonyl
-cyclohexyl)methyl
82. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂
83. Ac-pAph-Pgl-[Pal(3)Me]PalMe(3)-NH₂
84. Ac-pAph-Chg-Pal(3)(CH₂COOH)-NH₂
85. (2-quin)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂
86. Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(4-carboxycyclohexyl)methyl
87. Ac-pAph-Chg-NH[4-(1-methyl-pyridinium)methyl]
88. (2-furoyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
89. (3,4-dichlorobenzoyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
90. (2-thienylacetyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
91. (N-(5-methyl-2-thienoyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
92. Ac-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
93. (Ethoxycarbonyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)

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94. (2-fluorobenzoyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
95. Ac-pAph-Chg-NH-(4-amidinobenzyl)
96. Alloc-pAph-Chg-NH-[4-(-methylpyridinium)-methyl]
97. (t-Butoxycarbonyl)-pAph-Chg-NH-(4-trimethyl-ammonium benzyl)
98. (2-furoyl)-pAph-Chg-NH-1-[3(N-methylpyridyl)]-1-(methylacetate)ethyl
99. Ac-pAph-Chg-NH-1-[3(N-methylpyridyl)]-1-(methylacetate)ethyl
100. Ac-pAph-Chg-NH-[1-(1-methyl-4-pyridinium)ethyl]
101. Ac-pAph-Chg-NH-[1-(1-methyl-4-pyridinium)methyl]
102. Ac-pAph-Chg-NH-[1-(1-methyl-4-pyridinium)-2-hydroxy]ethyl
103. CF₃C(O)-(iBu)-Tyr-Ile-Arg-NH₂
104. Ac-D-pAph-Chg-Arg-Leu-Pro-NH₂
105. Ac-D-pAph-Chg-Arg-Gla-Pro-NH₂
106. Ac-D-pAph-Chg-Arg-Cys(CH₂-COOH)-Pro-NH₂
107. Ac-D-pAph-Chg-Arg-N(carboxymethyl)Gly-Pro-NH₂
108. Ac-D-pAph-Chg-Arg-(carboxyethyl)Gly-Pro-NH₂
109. Ac-D-pAph-Chg-Arg-N[1(1,3-dicarboxy)propyl]Gly-Pro-NH₂
110. Ac-D-pAph-Ile-Arg-Leu-Pro-NH₂
111. Alloc-D-pAph-Chg-Arg-Leu-Pro-NH₂
112. Ac-D-pAph-Chg-[Pal(3)Me]PalMe(3)-Leu-Pro-NH₂
113. Ac-D-pAph-Chg-Arg-NH₂.

In the claims:

Please amend the claims as follows.

8. A compound selected from the group consisting of
 (2-benzofuroyl)-Tyr-Chg-Arg-Pen-Pro-NH₂;

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(2-benzofuroyl)-pAph-Chg-[Pal(3)Me]PalMe(3)-Pen(CH₂COOH)-Pro-NH₂;
Ac-pAph-Chg-Arg-Cys(CH₂COOH)-Pro-NH₂;
(Alloc)-pAph-Chg-Arg-Leu-Pro-NH₂;
(2-benzofuroyl)-pAph-Chg-Arg-Pen(CH₂COOH)-Pro-NH₂;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-Pen(CH₂COOH)-Pro-NH₂;
Ac-pAph-Chg-Arg-Leu-Pro-NH₂; Ac-pAph-Chg-Arg-(HOOC-CH₂)Gly-Pro-NH₂;
Ac-pAph-Chg-Arg(HOOC-CH₂-CH₂)Gly-Pro-NH₂;
Ac-pAph-Chg-Arg-Gla-Pro-NH₂; Ac-pAph-Chg-Arg-Cys(CH₂-COOH)-Pro-NH₂;
Ac-Pal(4)Me-Chg-Arg-Leu-Pro-NH₂; Ac-(iBu)Nal(2)-Chg-Arg-Leu-Pro-NH₂;
Ac-Phe(p-CONH₂)-Chg-Arg-Leu-Pro-NH₂;
Ac-pAph-Chg-Arg-N[1(1,3-dicarboxy)propyl]Gly-Pro-NH₂;
Ac-pAph-Chg-Dap(CH=N(CH₃)₂)-Leu-Pro-NH₂;
(2-quinolinoyl)-Phe(NH₂)-Chg-Arg-Leu-Pro-NH₂;
Ac-pAph-Chg-Arg-N(carboxymethyl)Gly-Pro-NH₂;
Ac-pAph-Chg-Arg-(carboxyethyl)Gly-Pro-NH₂; Ac-mAph-Chg-Arg-Leu-Pro-NH₂;
Alloc-pAph-Chg-[Pal(3)Me]PalMe(3)-Pen(CH₂COOH)-Pro-NH₂;
Ac-pAph-Chg-Arg-N[1(1,3-dicarboxy)propyl]Gly-Pro-NH₂;
Ac-pAph-Ile-Arg-Leu-Pro-NH₂; Ac-Phe(pNH₂)-Chg-Arg-(Me)Leu-Pro-NH₂;
Ac-(Chx-CH₂)Tyr-Chg-Arg-Leu-Pro-NH₂;
(3-pyridoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
(3-pyridoyl)-Nal(2)-Chg-Arg-Leu-Pro-NH₂;
Ac-Pal(4)Me-Chg-Pal(4)Me-Leu-Pro-NH₂; Alloc-pAph-Chg-Arg-Leu-Pro-NH₂;
(4-isoquinolinoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
Ac-pAph-Cha-[Pal(3)Me]PalMe(3)-(Me)Leu-Pro-NH₂;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-Leu-Pro-NH₂;

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(2-naphthyl-CH₂)Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
 (5-pyrazinoyl)Nal(2)-Chg-Arg-Leu-Pro-NH₂;
 (Benzoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
 Ac-(2-methylpentanyl)-Tyr-Ile-Arg-Leu-Pro-NH₂;
 (2-pyridonyl)Phe(pNH₂)Chg-Arg-Leu-Pro-NH₂;
 (Benzoyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
 Ac-(2-methylpentyl)Tyr-Ile-Arg-Leu-Pro-NH₂;
 Ac-(iBu)Phe(pCN)-Chg-Arg-Leu-Pro-NH₂;
 Ac-(2-methylbutyl)Tyr-Ile-Arg-Leu-Pro-NH₂;
 Ac-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂; Ac-Phe(pNH₂)-Chg-Arg-Leu-Hyp-NH₂;
 Ac-Tyr-Chg-Arg-Leu-Pro-NH₂;
 (2-naphthylsulfonyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
 (2-methylbenzyl)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂;
 (2-benzofuroyl)-Phe(pNH₂)-Chg-Dab(CH=N(CH₃)₂)-Leu-Pro-NH₂;
 Ac-(cyclopentenyl-CH₂)Tyr-Ile-Arg-Leu-Pro-NH₂;
 Ac-Pal(4)Me-Chg-[Pal(3)Me]PalMe(3)-Leu-Pro-NH₂;
 Ac-(iBu)-Phe(pNH₂)-Chg-Arg-Leu-Pro-NH₂; and
 Ac-(Chx-CH₂)-Tyr-Ile-Arg-Leu-Pro-NH₂.

9. A compound selected from the group consisting of
 Ac-pAph-Chg-Arg-Leu-NH₂ and Ac-pAph-Chg-Arg-[Leu-OH]Leu.

10. A compound selected from the group consisting of
 (2-benzofuroyl)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂ and Ac-(iBu)Phe(pNH₂)-Chg-Arg-NH₂.

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11. A compound selected from the group consisting of
Alloc-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂;
(2-quinolinoyl)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH(1-methoxycarbonyl)-1-cyclohexyl;
Ac-pAph-Chg-Arg-NH₂; (2-pyridoyl)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂;
CF₃C(O)-(iBu)Phe(pNH₂)-Chg-Arg-NH₂;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(1-methoxycarbonyl)-1-cyclopentyl;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(4-methoxycarbonyl-cyclohexyl)methyl;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(3-thienyl-2-carboxylic acid methyl ester);
Ac-pAph-Chg-Arg-NH₂; CF₃C(O)-(iBu)Tyr-Chg-Arg-OH;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(4-methoxycarbonyl-cyclohexyl)methyl;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂; Ac-pAph-Chg-Pal(3)(CH₂COOH)-NH₂;
(2-quinolinecarboxy)-pAph-Chg-[Pal(3)Me]PalMe(3)-NH₂;
Ac-pAph-Chg-[Pal(3)Me]PalMe(3)-NH-(4-carboxycyclohexyl) methyl; and
CF₃C(O)(iBu)-Tyr-Ile-Arg-NH₂.
20. A compound selected from the group consisting of
Ac-D-pAph-Chg-Arg-Leu-Pro-NH₂; Ac-D-pAph-Chg-Arg-Gla-Pro-NH₂;
Ac-D-pAph-Chg-Arg-Cys(CH₂-COOH)-Pro-NH₂;
Ac-D-pAph-Chg-Arg-N(carboxymethyl)Gly-Pro-NH₂;
Ac-D-pAph-Chg-Arg-(carboxyethyl)Gly-Pro-NH₂;
Ac-D-pAph-Chg-Arg-N[1(1,3-dicarboxy)propyl]Gly-Pro-NH₂;
Ac-D-pAph-Ile-Arg-Leu Pro-NH₂;
Alloc-D-pAph-Chg-Arg-Leu-Pro-NH₂;
Ac-D-pAph-Chg-[Pal(3)Me]PalMe(3)-Leu-Pro-NH₂; and
Ac-D-pAph-Chg-Arg-NH₂.

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25. A method of specifically inhibiting the activity of Factor Xa, comprising contacting the factor Xa with the compound as in [of] claims [2] 7, 8, 9, 10, 11, 20, 21, 22, or 23.

M:\CDahling\Aventis Pharma Deutschland GmbH\P26.835-USA\Reply to Final Action Final.wpd